European Commission Approves Gilead Sciences' Tybost™, a New Boosting Agent for HIV Therapy

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– Tybost Facilitates Once-Daily Dosing of the Protease Inhibitors Atazanavir and Darunavir –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Sep. 25, 2013-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the European Commission has granted marketing authorization for once-daily Tybost™ (cobicistat 150 mg tablets), a pharmacokinetic enhancer that boosts blood levels of certain HIV medicines. Tybost is indicated as a boosting agent for the HIV protease inhibitors atazanavir 300 mg once daily and darunavir 800 mg once daily as part of antiretroviral combination therapy in adults with HIV-1 infection. Today's approval allows for the marketing of Tybost in all 28 countries of the European Union (EU).

"Gilead is pleased to offer HIV patients who rely on protease inhibitors a new boosting option to help facilitate once-daily dosing – an important factor in supporting treatment adherence," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences.

The EU approval of Tybost is supported by 48-week data from a pivotal Phase 3 study (Study 114), which found that Tybost was non-inferior to ritonavir when administered with an antiretroviral regimen of atazanavir plus Truvada® (emtricitabine 200 mg and tenofovir disoproxil (as fumarate) 245 mg) in HIV-infected treatment-naïve adults. Approval is also supported by pharmacokinetic data demonstrating that Tybost boosts blood levels of atazanavir and darunavir similar to ritonavir. Tybost should only be co-administered with atazanavir or darunavir.

In Study 114, Tybost was well tolerated and most adverse events were mild to moderate. The most common adverse reactions (incidence greater than or equal to 10 percent, all grades) were jaundice, ocular icterus and nausea.

Tybost is a component of Gilead's Stribild® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil (as fumarate) 245 mg), a once-daily complete single tablet regimen for the treatment of HIV-1 infection that was approved in the United States in August 2012 and in the European Union in May 2013. Gilead submitted a new drug application to the U.S. Food and Drug Administration (FDA) for Tybost as a single agent in June 2012 and received a Complete Response Letter in April 2013. Gilead is working on resubmitting the application to the FDA. Tybost is approved as a single agent in Canada.

About Tybost

Tybost is a cytochrome P450 3A (CYP3A) inhibitor. It boosts blood levels of atazanavir and darunavir by suppressing CYP3A, an enzyme that metabolizes these drugs in the body. Tybost acts only as a pharmacokinetic enhancer and has no antiviral activity.

Indication and Important Safety Information about Tybost

Tybost is indicated as a pharmacokinetic enhancer of atazanavir 300 mg once daily or darunavir 800 mg once daily as part of antiretroviral combination therapy in human immunodeficiency virus-1 (HIV-1) infected adults.

Co-administration with the following medicinal products is contra-indicated due to the potential for serious and/or life-threatening events or loss of therapeutic effect:

• alpha 1 adrenoreceptor antagonists: alfuzosin

• antiarrhythmics: amiodarone, quinidine

• anticonvulsants: carbamazepine, phenobarbital, phenytoin

• antimycobacterials: rifampicin

• ergot derivatives: dihydroergotamine, ergometrine, ergotamine

• gastrointestinal motility agents: cisapride

• herbal products: St. John’s wort (*Hypericum perforatum*)

• HMG-CoA reductase inhibitors: lovastatin, simvastatin

• neuroleptics: pimozide

• PDE-5 inhibitors: sildenafil for treatment of pulmonary arterial hypertension

• sedatives/hypnotics: orally administered midazolam, triazolam

Cobicistat is a strong mechanism-based CYP3A inhibitor and is a CYP3A substrate. Increased plasma concentrations of medicinal products that are metabolised by CYP3A (including atazanavir and darunavir) are observed on co-administration with cobicistat. Higher plasma concentrations of co-administered medicinal products can result in increased or prolonged therapeutic effects or adverse reactions. For medicinal products metabolised by CYP3A these higher plasma concentrations may potentially lead to severe, life-threatening or fatal events. Co-administration of Tybost and atazanavir or darunavir with products that induce CYP3A is not recommended because the resulting levels of cobicistat could be insufficient to achieve adequate pharmacoenhancement of atazanavir or darunavir. Co-administration of Tybost with medicinal products that inhibit CYP3A may decrease the clearance of cobicistat, resulting in increased cobicistat plasma concentrations. Cobicistat is a weak CYP2D6 inhibitor and is metabolised to a minor extent by CYP2D6. Co-administration with cobicistat can increase plasma concentrations of medicinal products that are metabolised by CYP2D6. Cobicistat inhibits the transporters p-glycoprotein (P-gp), BCRP, MATE1, OATP1B1 and OATP1B3. Co-administration of Tybost in patients receiving medicinal products that are substrates of these transporters may result in increased plasma concentrations of the co-administered medicinal products. Unlike ritonavir, cobicistat is not an inducer of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19 or UGT1A1. If switching pharmacoenhancers from ritonavir to cobicistat, caution is required during the first two weeks of treatment with Tybost, particularly if doses of any concomitantly administered medicinal products have been titrated or adjusted during use of ritonavir as a pharmacoenhancer.

No dosing recommendations can be made regarding the use of Tybost with oral contraceptives. Alternative forms of contraception should be considered.

Tybost must be co-administered with either atazanavir 300 mg once daily or with darunavir 800 mg once daily. Safety and efficacy have not been established for use of Tybost with either atazanavir or darunavir when used in any other dosing regimen. Antiviral efficacy data from randomized controlled studies is available for cobicistat-boosted atazanavir, but not for cobicistat-boosted darunavir.

Tybost must not be used as a pharmacokinetic enhancer of any other HIV-1 protease inhibitor or any other antiretroviral medicinal product that requires boosting since dosing recommendations for such co-administration have not been established and may result in insufficient plasma level of the antiretroviral medicinal product(s) leading to loss of therapeutic effect and development of resistance.

Tybost co-administered with atazanavir or darunavir should not be used in combination with another antiretroviral agent that requires pharmacoenhancement by means of co-administration with an inhibitor of CYP3A4 to reach the desired therapeutic plasma concentrations (i.e., another protease inhibitor or elvitegravir). Dosing recommendations for such combinations have not been established and co-administration may result in decreased plasma concentrations of atazanavir, darunavir and/or the other antiretroviral agents that require pharmacoenhancement leading to loss of antiviral activity and development of resistance. Tybost should not be used concurrently with ritonavir due to similar effects of cobicistat and ritonavir on CYP3A. Tybost should not be used in combination with other medicinal products containing cobicistat (such as the fixed dose combination tablet elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil (as fumarate)).

Cobicistat has been shown to decrease estimated creatinine clearance due to inhibition of tubular secretion of creatinine. This effect on serum creatinine, leading to a decrease in the estimated creatinine clearance, should be taken into consideration when Tybost is administered to patients in whom the estimated creatinine clearance is used to guide aspects of their clinical management, including adjusting doses of co-administered medicinal products. Tybost should not be initiated in patients with creatinine clearance less than 70 ml/min if one or more co-administered agent requires dose adjustment based on creatinine clearance (e.g. emtricitabine, lamivudine, tenofovir disoproxil (as fumarate) or adefovir). There are currently inadequate data to determine

whether co-administration of tenofovir disoproxil (as fumarate) and cobicistat is associated with a greater risk of renal adverse reactions compared with regimens that include tenofovir disoproxil (as fumarate) without cobicistat.

Cobicistat has not been studied in patients with severe hepatic impairment (Child Pugh Class C). Therefore, the use of Tybost is not recommended in these patients.

Tybost contains the azo colouring agent sunset yellow FCF (E110), which may cause allergic reactions.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Asia Pacific.

Forward-Looking Statement

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties and other factors, including the risk that physicians may not see advantages of Tybost over ritonavir and may therefore be reluctant to prescribe the product. In addition, pending marketing applications for Tybost in the United States and other regions may not be approved or approval may be delayed, and marketing approvals, if granted, may have significant limitations on their use. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

EU Summary of Product Characteristics for Tybost, Stribild and Truvada are available at http://www.ema.europa.eu.

Tybost, Stribild and Truvada are trademarks or registered trademarks of Gilead Sciences, Inc.

For more information on Gilead Sciences, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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